REMARKS

Reconsideration is requested.

The Examiner is requested to see the Preliminary Amendment of September 30, 2005, wherein the cross-reference to prior applications was inserted. See §7. on page 3 of the Office Action dated September 24, 2010.

Claims 1-30 are pending.

The objections to claims 2-6, 8, 10-22, 24, 26-28 and 30 are obviated by the above amendments. Withdrawal of the objections is requested.

The undersigned has been advised that the applicants' overseas agent is obtaining a newly executed Declaration, which will be filed separately under separate cover once received, in response to the Examiner's comments in §6. on page 4 of the Office Action dated September 24, 2010.

The Rule 75 objection of claims 4-22 and 26-30 is traversed. The Examiner is requested to appreciate that the Preliminary Amendment of September 30, 2005 amended the objected to claims to be singly dependent. Withdrawal of the objection is requested.

The Section 112, second paragraph, rejection of claim 29 is obviated by the above amendments. The claims are submitted to be definite. Withdrawal of the Section 112, second paragraph, rejection is requested.

The Section 102 rejection of claims 1-8, 10-12 and 14 over Shakesheff (WO 02/47557 A1) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing remarks.

Shakesheff discloses a nerve regeneration conduit which comprises a lumen filled with a hydrogel, such as collagen. The small internal diameter of the conduit is reported to accelerate the extension of neurites through the conduit.

However, the nerve regeneration conduit of Shakesheff does contain all the features of the claimed tissue growth guides. The cited art does not anticipate the pending claims.

The claims require that tissue growth guides of the claims contain an inner core and an outer sheath. The inner core comprises a biopolymer matrix which is fixed to the outer sheath in at least two places (a “first attachment region” and a “second attachment region”).

There is no disclosure or suggestion in Shakesheff of the fixing of the hydrogel in the lumen to the conduit. Nor is there any teaching which could be interpreted as such. For example, in the experimental section of Shakesheff, glass conduits made from 3mm lengths of glass micropipette are filled with collagen lattice solution, which is then gelled (pages 6-7). There is nothing which suggests or implies that the gelled collagen is fixed or attached to the conduit in any way. Nor is there any teaching which might suggest to the ordinarily skilled person how the collagen gel could be attached to the glass micropipette.

The absence of attachment is significant. Even if a tensile force was applied to the hydrogel of the nerve regeneration conduit of Shakesheff, this force would not generate mechanical tension within the hydrogel because the hydrogel is free to move relative to the conduit. The application of a tensile force to the hydrogel would simply result in a cell-compacted hydrogel within the lumen of the conduit.

The Examiner appears to allege that the absence of nutrients within the hydrogel filled lumen of the conduit somehow imparts a mechanical tension which allegedly allows neurites to grow along the conduit. However, there is no basis for such an interpretation in the cited art. Page 3 of Shakesheff states:

> "Without being bound by theory, the Applicant believe that conduits having substantially impermeable walls may promote growth of the neurites within the conduit by denying them nutrients, whereby the neurites are encouraged to grow along the conduit towards a distal end. In this regard, growth factors may be disposed at or adjacent a distal opening of the or each conduit."

One of ordinary will appreciate the cited art to teach in this regard that walls which are impermeable to nutrients encourage neurites in the conduit to grow towards the distal end of the conduit, where nutrients can be accessed. There is no mention or teaching in the cited art however of mechanical tension and no reason why mechanical tension would be generated in this situation.

Furthermore, the inner core of tissue growth guides of the claims contains cells which impart the mechanical tension between the attachment regions. By contrast, the hydrogel in the lumen of the conduits of the cited art is devoid of cells. The Examiner suggests that:

> "neuritis [sic] are undifferentiated axon or dendrites within a cell culture and are therefore neuroblasts." See page 6 of the Office Action dated September 24, 2010

One of ordinary skill would not agree with the Examiner's definition in this regard. Rather, one of ordinary skill will appreciate that a neurite is a projection from the cell body of a neuron and may either be an axon (which conducts action potentials away from the cell body) or a dendrite, (which conducts action potentials towards the cell body). Since Shakesheff relates to "nerve regeneration", one of ordinary skill will appreciate that this is what Shakesheff means by a "neurite".

The term "neurite" has nothing to do with neuroblasts, which are neural progenitor cells.

According to the teaching of Shakesheff, neurites grow through the hydrogel in the lumen of the conduits. However, these neurites project from cell bodies which are located outside the conduit (see Figure 6 of Shakesheff). There is no disclosure in Shakesheff of the cells themselves being inside the conduit, as required by the present claims. The conduits of Shakesheff may contain neurites but they do not contain cells. In the absence of cells within the hydrogel, the conduits of Shakesheff lack any means by which tension could be generated in the hydrogel, even if the hydrogel were fixed to the sheath at first and second attachment regions.

The lumen of the conduits of Shakesheff does not contain cells and is not fixed to the outer sheath at first and second attachment regions, as required by the present claims. Unlike the tissue growth guides of the present claims, the Shakesheff conduits therefore lack both tension and the means to generate and sustain tension (e.g. cells

and attachment regions). The tissue growth guides of the claims are therefore not anticipated by the conduits of Shakesheff.

Withdrawal of the Section 102 rejection is requested.

The Section 103 rejection of claims 1-21 and 23-25 over Kadiyala (U.S. Patent No. 6,174,333 B1) Shakesheff (WO 02/47557 A1) and Chen (Biomaterials, Vol. 21, pp 1541-1547, 2000) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following distinguishing comments.

The Examiner asserts that

> "it would have been prima facie obvious to a person of ordinary skill in the art at the time the claimed invention was made and said artisan would have been motivated to combine the teachings from Kadiyala et ai., with those of Shakesheff et al., and Chen et al.,; because each of Shakesheff et al., and Chen et al., teach a nerve regenerating device wherein a gel matrix comprising the nerve cells is enclosed in a sheath and Chen et al., further describe said sheath to be made of silicone, i.e., biosorbable material." See page 10 of the Office Action dated September 24, 2010.

It would not have been obvious to combine the cited art as alleged by the Examiner to have made the claimed invention. The combination of references fails to teach or suggest the elements of the instant claims and a skilled person would not have combined the cited references in such as way as to arrive at the claimed invention.

.Kadiyala teaches an implant which comprises a contracted cell-seeded gel matrix which has a suture embedded within it. During production of the implant, the suture is held in tension with a spring. The opposition of the spring to the contraction

mediated by cells within the matrix produces tension and causes alignment of the cells and matrix fibres. This is evident from col 4 lines 41-46 of Kadiyala, which states:

> "The tension applied to the gel matrix while the gel is being contracted (which as shown In FIG. 2 can be applied by tension wire 45 18) causes the cells within the matrix to align in the direction in which tension is applied to the matrix"

Significantly, once the gel matrix is contracted and the cells and matrix fibres aligned, the spring is removed, so that the implant is no longer under tension. According to Kadiyala, the implant is only ready for implantation after removal of the spring. This is shown in figures 1, 3-5, 7 and col 5 lines 45-50, which states (emphasis added):

> "At the 4 hour time point, the gel was firmly attached to the central suture, such that the suture and tension spring could be lifted out of the medium, the tension spring removed, and the gel implanted in the surgical defect as described"

The tension spring is therefore removed after contraction, and is not present in the finished implant, which is no longer under tension. There is neither teaching nor suggestion in Kadiyala to implant the contracted gel with the tension spring still in place.

Furthermore, the instant claims require the presence of an "outer sheath which surrounds the inner core". The tension spring of Kadiyala would not be interpreted by one of ordinary skill to be an "*outer sheath which surrounds the inner core*" as required by the instant claims.

Kadiyala therefore lacks any teaching or suggestion of an inner core which is fixed to an outer sheath at two separate attachment regions, as required by the present claims.

Neither Chen nor Shakesheff remedies these deficiencies of the primary reference. The combination of Kadiyala, Chen and Shakesheff fails to suggest the claimed invention. The ordinarily skilled person would not have combined the cited art to have made the claimed invention.

Combination of the cited art would have, at best, resulted in a gel matrix which is contracted around a suture using a tension spring, as taught by Kadiyala and then enclosed in a sheath as taught by Chen and Shakesheff. Such a construct would not have had however, for example, an inner core which is fixed to an outer sheath at two separate attachment regions, as required by the present claims.

One of ordinary skill would not have been motivated by the cited combination of art to have made a self-tensioning tissue growth guide.

Withdrawal of the Section 103 rejection based on Kadiyala, Shakesheff and Chen is requested.

The Section 103 rejection of claim 22 over Kadiyala, Shakesheff, Chen and Nyberg (Biotechnology and Bioengineering, Vol. 41, pp 194-203, 1993) is traversed. Reconsideration and withdrawal of the rejection are requested as the deficiencies of the combination of Kadiyala, Shakesheff and Chen, such as are described above, are not cured by the teachings of Nyberg.

The Section 103 rejection of claims 26-30 over Kadiyala, Shakesheff, Chen is traversed. Clarification is requested regarding the basis of the rejection in the event same is maintained as the Examiner has referred to Kadiyala (U.S. Patent No.

6,174,333 A1) and Shakesheff (WO 02/47557 A1) as being both primary and "additional" references. See §18. on page 12 of the Office Action dated September 24, 2010. Reconsideration and withdrawal of the rejection are requested for at least the reasons noted above with regard to the rejection of claims 1-21 and 23-25 over Kadiyala, Shakesheff, Chen. Withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /B. J. Sadoff/
B. J. Sadoff
Reg. No. 36,663

BJS:pp
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100